File Reference: 059893-0115

IN THE INTERNATIONAL BUREAU OF WIPO
UNDER THE PATENT COOPERATION TREATY

Applicants	:	MERCK & CO., INC.
International Application No.	:	PCT/US2005/001469
International Filing Date	:	January 14, 2005 (14.01.2005)
Title of the Invention	:	**NPC1L1 (NPC3) AND METHODS OF IDENTIFYING LIGANDS THEREOF**

STATEMENT UNDER ARTICLE 19(1)

The International Bureau of WIPO
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1211 Geneva 20
SWITZERLAND

Attn: Shafiqul Haq

Dear Sir or Madam:

One or more claims as filed are being amended as follows:

Applicant has amended Claims 6, 9, 10 and 20 to include structures for Formulas I and II and compound 2. Support for this amendment can be found at pages 32, line 20, page 33, line 7 and page 83, line 1.

The foregoing amendments do not go beyond the disclosure as originally filed.

Respectfully submitted,

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Date: May 12, 2006

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CLAIMS

1. A method for identifying a ligand of NPC1L1 comprising:

contacting human NPC1L1 with a detectably labeled substituted 2-azetidinone glucuronide and a candidate compound; and

determining whether said candidate compound binds to human NPC1L1;

wherein binding of said candidate compound to human NPC1L1 modulates binding of said detectably labeled substituted 2-azetidinone glucuronide to human NPC1L1, wherein the detectably labeled substituted 2-azetidinone glucuronide has a binding affinity K_D value for human NPC1L1 that is 200nM or lower, and wherein said modulation indicates that the candidate compound is a ligand that binds to human NPC1L1.

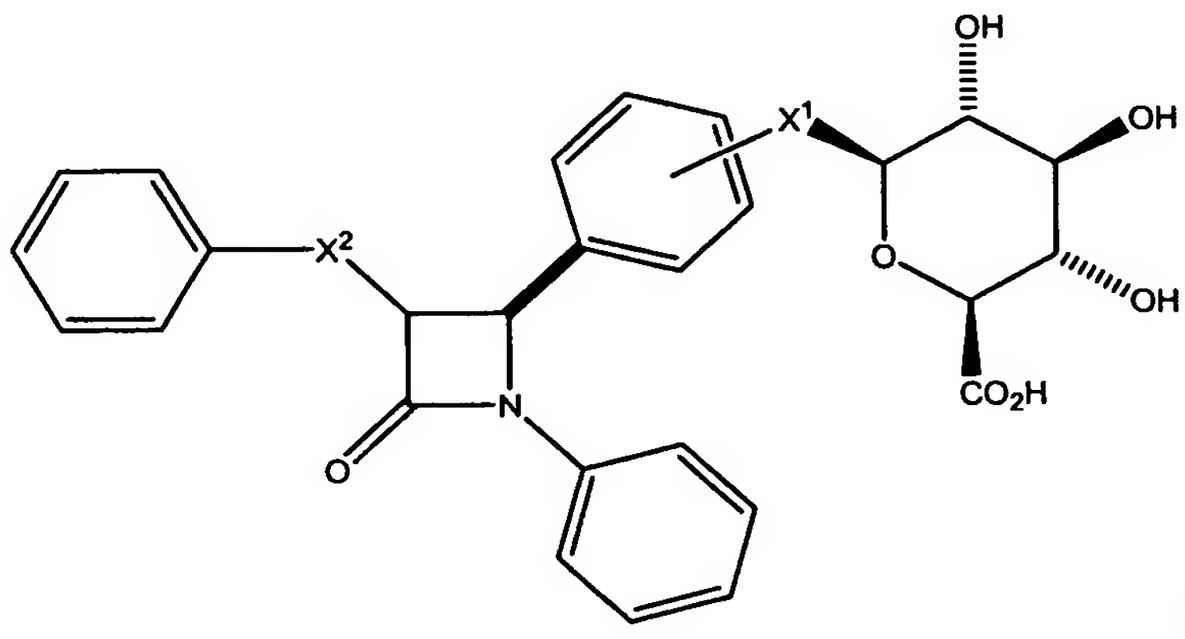
2. The method of claim 1, wherein the K_D value is 100nM or lower.

3. The method of claim 1, wherein the K_D value is 50nM or lower.

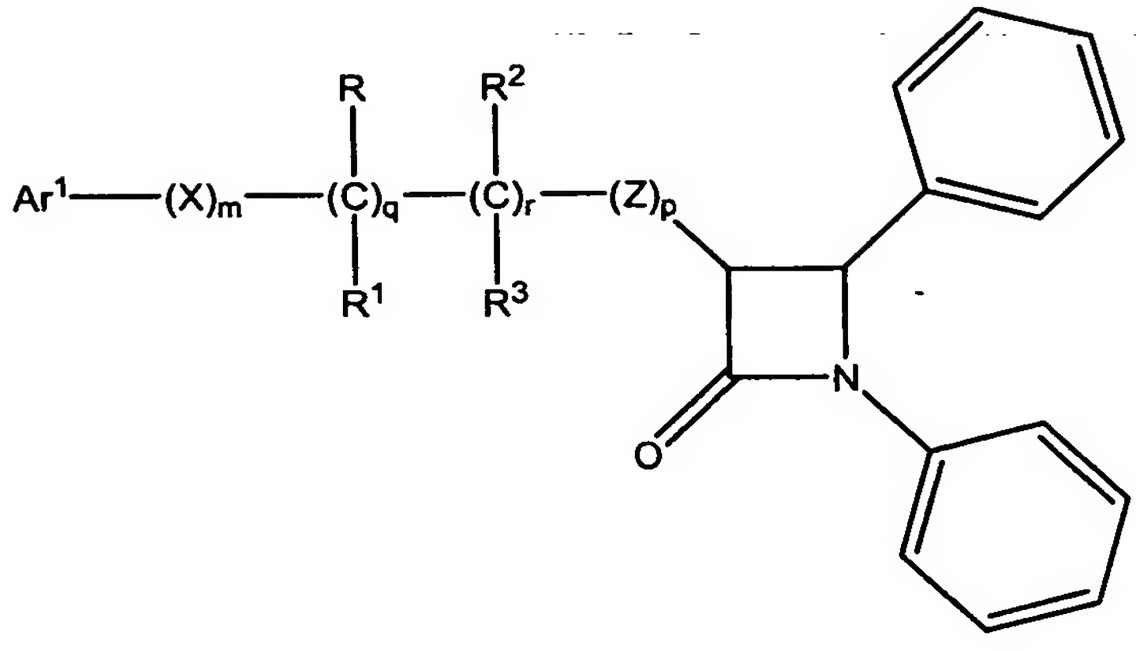
4. The method of claim 1, wherein the K_D value is 20nM or lower.

5. The method of claim 1, wherein the K_D value is 10nM or lower.

6. The method of claim 1, wherein the substituted 2-azetidinone-glucuronide is selected from the group consisting of a compound of Formula I and a compound of Formula II.



(I)

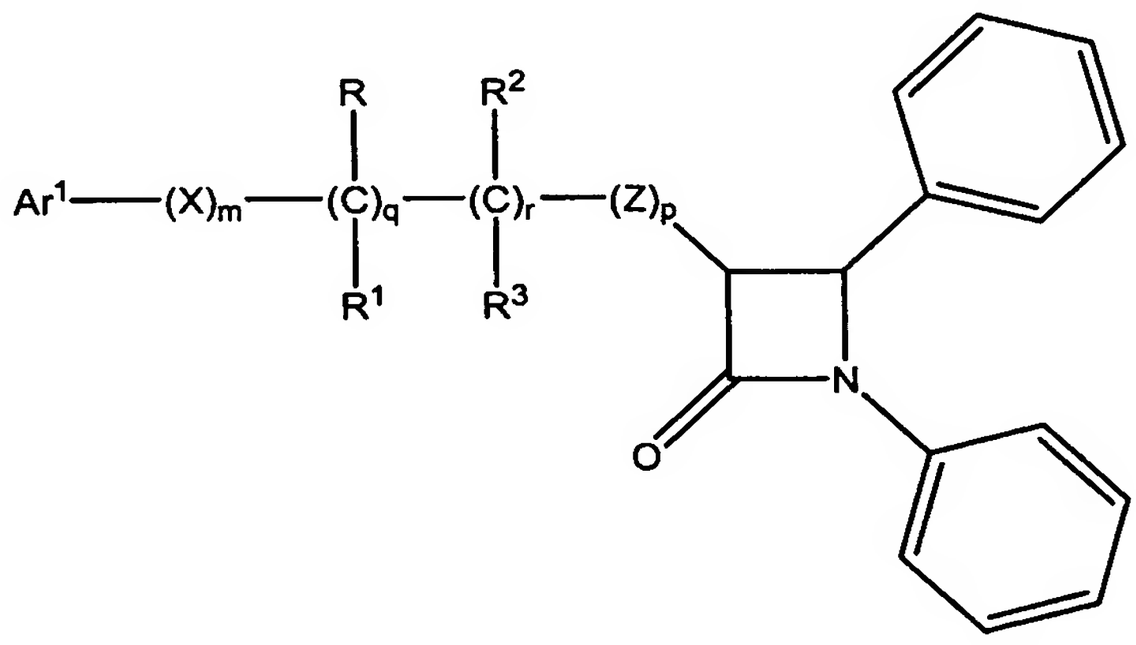


(II)

7. The method of claim 6, wherein the substituted 2-azetidinone-glucuronide comprises a detectable label from the group consisting of ^{35}S and ^{125}I.

8. The method of claim 7, wherein the detectable label is ^{35}S.

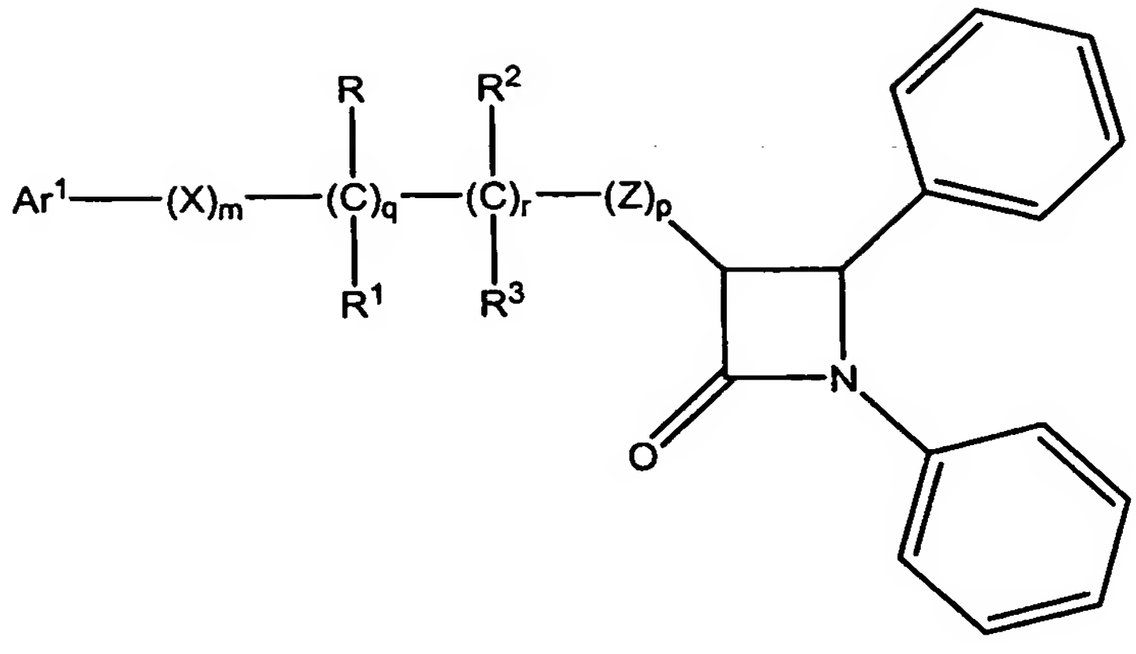
9. The method of claim 6, wherein the substituted 2-azetidinone-glucuronide is a compound of Formula II,



(II)

wherein R^9 comprises an $-SO_2-$ group.

10. The method of claim 9, wherein the substituted 2-azetidinone-glucuronide of Formula II



(II)

is labeled with ^{35}S.

11. A method for identifying a ligand of NPC1L1 comprising:

contacting human NPC1L1 with a detectably labeled substituted 2-azetidinone glucuronide of Formula II and a candidate compound; and

determining whether said candidate compound binds to human NPC1L1; wherein binding of said candidate compound to human NPC1L1 modulates binding of said detectably labeled substituted 2-azetidinone glucuronide of Formula II to human NPC1L1, and wherein said modulation indicates that the candidate compound is a ligand that binds to human NPC1L1.

12. The method of claim 11, wherein R^9 of the detectably labeled substituted 2-azetidinone glucuronide of Formula II comprises an $-SO_2-$ group.

13. The method of claim 11, wherein the detectably labeled substituted 2-azetidinone glucuronide of Formula II is labeled with ^{35}S.

14. The method of claim 11, wherein the detectably labeled substituted 2-azetidinone glucuronide of Formula II has a binding affinity K_D value for human NPC1L1 that is 200nM or lower.

15. The method of claim 14, wherein the K_D value is 100nM or lower.

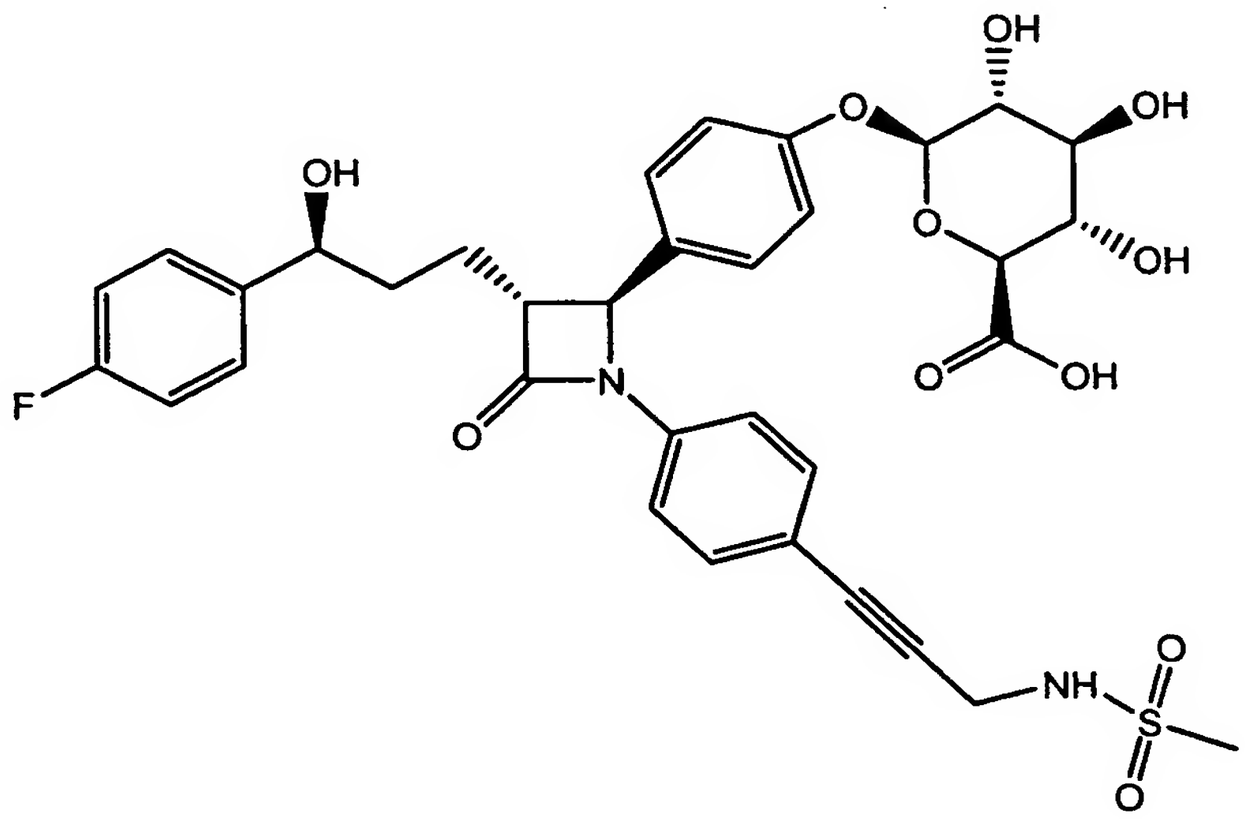
16. The method of claim 14, wherein the K_D value is 50nM or lower.

17. The method of claim 14, wherein the K_D value is 20nM or lower.

18. The method of claim 14, wherein the K_D value is 10nM or lower.

19. The method of claim 1 wherein the detectably labeled substituted 2-azetidinone glucuronide is labeled with ^{35}S.

20. The method of claim 1 wherein the detectably labeled substituted 2-azetidinone glucuronide is ^{35}S-labeled compound **2**



2.